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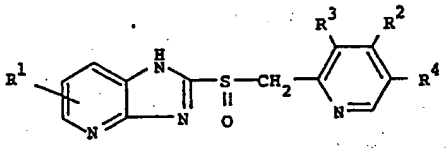
(54) Imidazo[4,5-b] pyridine compounds, process for preparing same and pharmaceutical compositions containing same.

(57) Imidazo[4,5-b]pyridine compounds of the general formula [I] are provided:



[I]

where R^1 is straight-chain or branched C_{1-8} alkoxy (which may be substituted with cycloalkyl) or C_{2-4} fluoroalkyloxy, R^2 is H, methyl or methoxy, and R^3 and R^4 are each H or methyl and may be the same or different. All these compounds exhibit good inhibition of potassium ion-dependent adenosine triphosphatase and excellent storage stability, so that they are usable for the treatment of gastric and/or duodenal ulcers.

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Description

IMIDAZO[4,5-b]PYRIDINE COMPOUNDS, PROCESS FOR PREPARING SAME AND PHARMACEUTICAL COMPOSITIONS CONTAINING SAME

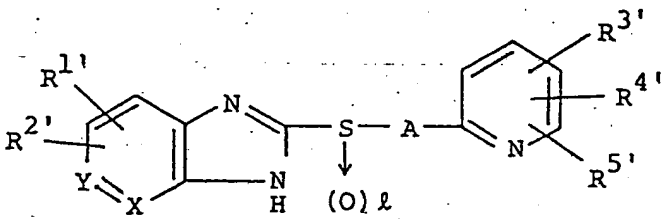
BACKGROUND OF THE INVENTION

(1) Field of the Invention

This invention relates to novel imidazo[4,5-b]pyridine compounds. The imidazo[4,5-b]pyridine compounds of this invention have excellent storage stability and can be used as drugs for the treatment of gastric and duodenal ulcers.

(2) Description of the Prior Art

In recent pathophysiological studies on gastric and duodenal ulcers, attention has been focused on the behavior of potassium ion-dependent adenosine triphosphatase [hereinafter referred to as (H+ + K+) ATPase] participating in the production of hydrochloric acid in the vesicles of the gastric endoplasmic reticulum, and the presence of an inhibitory effect on this enzyme is now considered to be a criterion of the usefulness of anti-ulcer agents (Gastroenterology, Vol. 1, p. 420, 1943; ibid., Vol. 73, p. 921, 1977). From this point of view, a class of compounds having a side chain comprising an unsubstituted to trisubstituted pyridylmethylsulfinyl group are now being developed as anti-ulcer agents, and one typical example thereof is Omeprazole having a benzimidazole skeleton (Japanese Patent Laid-Open No. 141783/'79; British Medical Journal, Vol. 287, p. 12, 1983). On the other hand, it has been confirmed or suggested that certain imidazopyridine compounds have an inhibitory effect on the aforesaid enzyme. Typical examples thereof are compounds of the general formula



where one of X and Y is =CH- and the other is =N-, $R^{1'}$ and $R^{2'}$ are each a hydrogen atom, a lower alkoxycarbonyl group, a halogen atom, a lower alkyl group, an amino group or a hydroxyl group and may be the same or different, $R^{3'}$, $R^{4'}$ and $R^{5'}$ are each a hydrogen atom, a lower alkoxy group or a lower alkyl group and may be the same or different, A is a lower alkylene group, and ℓ is 0 or 1. However, when Y is =CH-, X is =N-, and ℓ is 0, $R^{3'}$, $R^{4'}$ and $R^{5'}$ should not all be hydrogen atoms. These compounds are reported in Japanese Patent Laid-Open No. 145182/'86 and will hereinafter be referred to tentatively as the well-known imidazopyridine compounds.

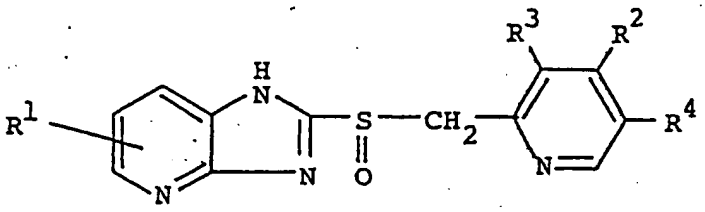
However, it has been found that, when stored without any preventive measure, Omeprazole undergoes a higher degree of deterioration than might be expected. In order to overcome its low storage stability, it has been imperative to convert Omeprazole into its alkali salt (Japanese Patent Laid-Open No. 167587/'84).

As to the well-known imidazopyridine compounds, the present inventors chose, as two typical examples thereof, 2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-6-bromoimidazo[4,5-b]pyridine (hereinafter referred to tentatively as Compound α) and 2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-6-methylimidazo[4,5-b]pyridine (hereinafter referred to tentatively as Compound β), and subjected them to various tests. As a result, it has been found that (1) similarly to Omeprazole, these compounds are also defective in storage stability and (2) while they exhibit a marked inhibitory effect on (H+ + K+) ATPase in the in vitro tests, this effect is not satisfactorily reflected in the in vivo tests for inhibitory effect on gastric secretion and for inhibitory effects on various experimental ulcers.

SUMMARY OF THE INVENTION

In view of these circumstances, the present inventors have made an exhaustive study of compounds related to the aforesaid well-known imidazopyridine compounds and have discovered that compounds obtained by substituting various alkoxy groups for the bromine atom or methyl group of Compounds α and β have excellent storage stability and exhibit a good anti-ulcer effect in various in vivo tests. The present invention has been completed on the basis of this discovery.

According to one feature of the present invention, there are provided imidazo[4,5-b]pyridine compounds of the general formula



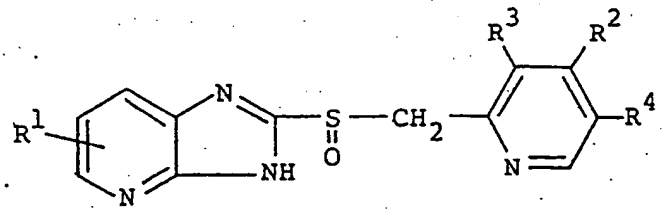
[I]

where R^1 is a straight-chain or branched alkoxy group of 1 to 8 carbon atoms (which may be substituted with a cycloalkyl group which preferably contains 3 to 6 carbon atoms) or a fluoroalkyloxy group of 2 to 4 carbon atoms, R^2 is a hydrogen atom, a methyl group or a methoxy group, and R^3 and R^4 are each a hydrogen atom or a methyl group and may be the same or different.

According to another feature of the present invention, there are provided processes for preparing imidazo[4,5-b]pyridine compounds represented by the above general formula [I].

According to still another feature of the present invention, there are provided pharmaceutical compositions, containing an imidazo[4,5-b]pyridine compound represented by the above general formula [I], as an active ingredient.

It is to be understood that the imidazo[4,5-b]pyridine compounds represented by the general formula [I] also include their tautomers represented by the general formula



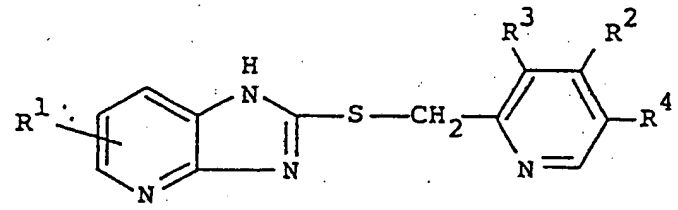
[I']

where R^1, R^2, R^3 and R^4 are as previously defined.

In the general formulae [I] and [I'], the alkoxy group represented by R^1 is selected from among methoxy, ethoxy, isopropyloxy, n-propyloxy, sec-butyloxy, isobutyloxy, tert-butyloxy, n-butyloxy, n-pentyloxy, 3-methylbutyloxy, n-hexyloxy, n-heptyloxy, 5-methylhexyloxy, 2,4,4-trimethylpentyloxy, n-octyloxy, cyclopropylmethyloxy, 1-cyclopropylethyloxy, cyclobutylmethyloxy, cyclopentylmethyloxy, 2-cyclopentylethyloxy, 3-cyclopentylpropyloxy, cyclohexylmethyloxy, 2-cyclohexylethyloxy and like groups. Similarly, the fluoroalkyloxy group represented by R^1 is selected from among 2,2,2-trifluoroethoxy, 2,2,3,3,3-pentafluoropropyloxy, 1,1,1,3,3,3-hexafluoro-2-propyloxy, 2,2,3,3,4,4,4-heptafluorobutyloxy and like groups.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

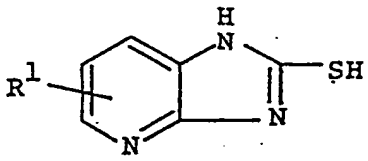
The imidazo[4,5-b]pyridine compounds represented by the above general formulas [I] and [I'] (hereinafter referred to briefly as the present compounds) can be prepared by oxidizing a sulfide compound of the general formula



[II]

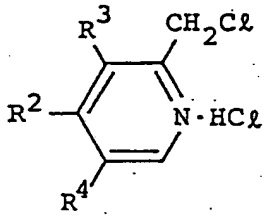
where R^1, R^2, R^3 and R^4 are as previously defined, in the presence of a suitable solvent and with the aid of an oxidizing agent. The oxidizing agent may be be used in an amount of 1.0 to 1.3 moles per mole of the sulfide compound [II]. Oxidizing agents useful for this purpose include, for example, peroxides such as m-chloroperbenzoic acid, perbenzoic acid, peracetic acid and the like. However, m-chloroperbenzoic acid is preferred because of its high stability. Suitable reaction solvents include, for example, halogenated hydrocarbons such as chloroform, tetrachloroethane, etc.; alcohols such as methanol, ethanol, propanol, butanol, etc.; and mixtures of two or more such solvents. However, from the viewpoint of selectivity and yield in the oxidation reaction, it is particularly preferable to use chloroform or a mixture of chloroform and methanol. The reaction is carried out at a temperature of -70 to 30°C, preferably -20 to 10°C, for a period of time ranging approximately from 1 minute to 24 hours, preferably from 5 minutes to 1 hour.

The sulfide compounds represented by the above general formula [II] can be prepared by condensing a thiol compound of the general formula



[III]

where R^1 is as previously defined, with a pyridine compound of the general formula



[IV]

where R^2, R^3 and R^4 are as previously defined, in a reaction solvent. This reaction may be carried out in the presence or absence of a base. If it is carried out in the absence of base, the resulting sulfide compound [II] is in the form of a hydrochloride and, therefore, needs to be dehydrochlorinated by means of a deacidifying agent. The pyridine compound [IV] may be used in an amount equimolar to the thiol compound [III], and the base may be used in an amount of 2.0 to 3.0 moles per mole of the thiol compound [III]. Bases useful for this purpose include, for example, sodium hydrogen carbonate, sodium carbonate, potassium carbonate, sodium hydroxide, potassium hydroxide and the like. Suitable reaction solvents include, for example, alcohols such as methanol, ethanol, propanol, butanol, etc.; aprotic polar solvents such as dimethylformamide, dimethyl sulfoxide, etc.; water; and mixtures of two or more such solvents. The reaction is carried out at a temperature of 10 to 200°C, preferably 60 to 80°C, for a period of time ranging approximately from 1 minute to 12 hours, preferably from 5 minutes to 4 hours. The thiol compound [III] used as a starting material can be prepared according to many well-known processes including, for example, that described in The Journal of Organic Chemistry, Vol. 24, p. 1455, 1959.

Now, the beneficial effects of the present compounds [I] will be described hereinbelow. Specifically, they were tested for storage stability, in vitro inhibitory effect on (H+ + K+) ATPase, and in vivo inhibitory effects on gastric secretion and on various experimental ulcers. The test compounds used for this purpose were the compounds enumerated below and considered to be typical examples of the present compounds [I]. The designation given in parentheses after the chemical name of each compound means its tentative name as used herein and corresponds to the respective one of the examples which will be described later.

2-[2-(3,5-Dimethyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine (Example 1).
2-[2-(3,5-Dimethyl-4-methoxy)pyridylmethylsulfinyl] 5-methoxyimidazo[4,5-b]pyridine (Example 2).
2-[2-(3,4,5-Trimethyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine (Example 3).
2-[2-(4-Methoxy-5-methyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine (Example 4).
2-[2-(4-Methoxy-5-methyl)pyridylmethylsulfinyl]-7-methoxyimidazo[4,5-b]pyridine (Example 7).
2-[2-(3,4,5-Trimethyl)pyridylmethylsulfinyl]-5-ethoxyimidazo[4,5-b]pyridine (Example 8).
2-[2-(3,5-Dimethyl)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine (Example 10).
2-[2-(3,4,5-Trimethyl)pyridylmethylsulfinyl]-5-n-butyloxyimidazo[4,5-b]pyridine (Example 12).
2-[2-(4-Methoxy-5-methyl)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine (Example 13).
2-[2-(3,5-Dimethyl)pyridylmethylsulfinyl]-5-ethoxyimidazo[4,5-b]pyridine (Example 14).
2-[2-(3,5-Dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine (Example 15).
2-[2-(4-Methoxy-5-methyl)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine (Example 16).
2-[2-(4-Methoxy)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine (Example 17).
2-[2-(3,5-Dimethyl)pyridylmethylsulfinyl]-5-n-propyloxyimidazo[4,5-b]pyridine (Example 18).
2-[2-(3,5-Dimethyl)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine (Example 19).
2-[2-(3,5-Dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine (Example 20).
2-[2-(4-Methoxy-5-methyl)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine (Example 21).
2-[2-(4-Methoxy)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine (Example 22).
2-[2-(3,5-Dimethyl)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine (Example 23).
2-[2-(3,5-Dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine (Example 24).
2-[2-(4-Methoxy)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine (Example 25).
2-[2-(3,5-Dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-(2,2,2-trifluoroethoxy)imidazo[4,5-b]pyridine (Example 26).
2-[2-(4-Methyl)pyridylmethylsulfinyl]-5-(2,2,3,3,4,4,4-heptafluorobutyloxy)imidazo[4,5-b]pyridine (Example

30).
2-[2-(3,5-Dimethyl)pyridylmethylsulfinyl]-5-n-heptyloxyimidazo[4,5-b]pyridine (Example 33).
2-[2-(3,5-Dimethyl)pyridylmethylsulfinyl]-5-(3-methylbutyloxy)imidazo[4,5-b]pyridine (Example 34).
2-[2-(3,5-Dimethyl-4-methoxy)pyridylmethylsulfinyl]-6-(3-cyclopentylpropyloxy)imidazo[4,5-b]pyridine (Example 36).

(i) Storage stability

The storage stability of the present compounds [I] was tested by allowing each test compound to stand under severe conditions (i.e., a temperature of 60°C and a relative humidity of 75%) for 8 days and then determining its percentage of residue according to a thin-layer densitometric method (Bunseki Kagaku, Vol. 23, No. 9, p. 1016, 1974). More specifically, upon completion of the severe treatment, 100 µg of each test compound was applied to a thin-layer plate and this plate was developed with a chloroform-ethanol mixture (volume ratio 10:1). The thin-layer plate used for this purpose was a TLC Plate Aluminum Oxide $60F_{254}$ (manufactured by Merck Co.; 0.25 mm in thickness and 20 cm x 20 cm in size), and it was developed over a distance of 15 cm. Then, using a Shimazu Two-wavelength Chromatoscanner CS-910 (manufactured by Shimazu Seisakusho), the resulting spot was analyzed at a wavelength of 300-315 nm.

The results thus obtained are shown in Table 1. For purposes of comparison, the percentages of residue of Omeprazole (at a measuring wavelength of 300 nm) and Compounds α and β (at a measuring wavelength of 310 nm) were determined in the same manner as described above and are also shown in Table 1.

Table 1

Test compound	Storage stability (after treatment at 60°C and 75% RH for 8 days)
	Percentage of residue
Omeprazole	3
Compound α	0
Compound β	9
Example 1	98
Example 2	77
Example 3	99
Example 4	98
Example 7	53
Example 8	96
Example 10	92
Example 12	76
Example 13	88
Example 14	93
Example 15	87
Example 16	90
Example 17	75
Example 18	85
Example 19	78
Example 20	72
Example 21	69
Example 22	57
Example 23	95
Example 24	94
Example 25	51
Example 26	92
Example 30	73
Example 33	89
Example 34	76
Example 36	68

As is evident from Table 1, it can be recognized that the present compounds [I] have much better storage stability than Omeprazole and Compounds α and β.

(ii) Inhibitory effect on (H+ + K+) ATPase

The inhibitory effect of the present compounds on (H+ + K+) ATPase was tested by adding each test compound to a solution containing 300-500 µg, on a protein basis, of the enzyme, incubating this reaction mixture at 35-37° C for 5-30 minutes, and then determining the residual activity of (H+ + K+) ATPase present in the reaction mixture. The test compounds were dissolved in methanol or ethanol in advance and added to the reaction system in such an amount as to give a concentration of 1×10^{-3} M. The (H+ + K+) ATPase used in this test was prepared from fresh pieces of the fundus ventriculi of hog stomach according to the method of Saccomani et al. (The Journal of Biological Chemistry, Vol. 251, No. 23, p. 7690, 1976). The residual activity of (H+ + K+) ATPase was determined by mixing magnesium chloride and potassium chloride with the incubated reaction mixture, adding adenosine triphosphate thereto, incubating this assay mixture 37° C for 5-15 minutes to effect an enzymic reaction, and colorimetrically determining the liberated inorganic phosphate by use of an ammonium molybdate reagent. The initial concentrations of magnesium chloride, potassium chloride and adenosine triphosphate were adjusted to 2 mM, 20 mM and 2 mM, respectively. Colorimetric determinations were made at a wavelength of 360-400 nm. As a control experiment, the residual activity of (H+ + K+) ATPase was determined by repeating the above-described procedure without adding any test compound to the reaction system. The results thus obtained are shown in Table 2. In this table, the inhibitory effect is indicated by the degree of inhibition which was obtained by calculating the difference between the measured value obtained in the control experiment and the measured value resulting from the addition of each test compound and expressing this difference as a percentage of the measured value obtained in the control experiment. For purposes of comparison, the inhibitory effect of Omeprazole and Compounds α and β on (H+ + K+) ATPase was tested in the same manner as described above and the results thus obtained are also shown in Table 2.

Table 2

Test compound	Inhibitory effect on $(H^+ + K^+)$ ATPase (at 1×10^{-3} M)
	Degree of inhibition (%)
Omeprazole	38.7
Compound α	100
Compound β	100
Example 1	100
Example 2	96.6
Example 3	100
Example 4	100
Example 7	98.8
Example 8	100
Example 10	90.0
Example 12	98.5
Example 13	87.4
Example 14	100
Example 15	98.5
Example 16	96.1
Example 17	93.7
Example 18	92.3
Example 19	100
Example 20	100
Example 21	97.4
Example 22	94.6
Example 23	100
Example 24	100
Example 25	92.9
Example 26	100
Example 30	92.1
Example 33	95.4
Example 34	98.5
Example 36	93.0

As is evident from Table 2, it can be recognized that the in vitro inhibitory effect of the present compounds [I] on (H+ + K+) ATPase is much better than that of Omeprazole and is comparable to that of Compounds α

and β.

(iii) Inhibitory effect on gastric acid secretion

The inhibitory effect of the present compounds [I] on gastric acid secretion was tested by using male Wistar rats, weighing about 200 g, in groups of five. To these rats which had been fasted overnight, the test compounds were orally administered in a series of appropriately selected doses ranging from 1 to 100 mg/kg. Then, the pyloric end of the stomach was ligated. After the lapse of 4 hours, the total acidity of gastric juice of each rat was measured. More specifically, the test compounds were suspended in a 0.5% aqueous solution of carboxymethyl cellulose and administered to the rats 30 minutes before ligation. Gastric juice was collected by sacrificing and laparotomizing each rat. The total acidity of gastric juice was determined by titrating the gastric juice with a 0.1 N aqueous solution of sodium hydroxide until a pH of 7.0 was reached. As a control experiment, the total acidity of gastric juice of an untreated group was determined in the same manner as described above. The inhibitory effect of the test compounds on gastric acid secretion was evaluated on the basis of the dose (in mg/kg) required to inhibit gastric acid secretion, i.e. the total acidity of gastric juice, by 50% (hereinafter referred to as ED_{50}). The ED_{50} value of each test compound was determined by calculating the difference in total acidity between the untreated group and each treated group, dividing the difference by the total acidity of the untreated group to obtain the degree of inhibition, and constructing a dose-response curve on the basis of the data thus obtained. The results are shown in Table 3. For purposes of comparison, the ED_{50} values of Omeprazole and Compounds α and β were determined in the same manner as described above and are also shown in Table 3.

Table 3

Test compound	Inhibitory effect on gastric acid secretion (p.o.) ED_{50} (mg/kg)
Omeprazole	35
Compound α	73
Compound β	41
Example 1	13
Example 2	18
Example 3	9
Example 4	15
Example 7	22
Example 8	12
Example 10	19
Example 12	21
Example 13	18
Example 14	15
Example 15	13
Example 16	16
Example 17	17
Example 18	19
Example 19	11
Example 20	10
Example 21	13
Example 22	15
Example 23	12
Example 24	9
Example 25	18
Example 26	15
Example 30	19
Example 33	17
Example 34	14
Example 36	19

As is evident from Table 3, it can be recognized that the present compounds [I] exhibit a more marked in vivo inhibitory effect on gastric acid secretion than Compounds α and β.

(iv) Inhibitory effects on various experimental ulcers

The inhibitory effects of the present compounds [I] on various experimental ulcers were tested by using male Wistar rats, weighing about 200 g, in groups of six and determining the respective ulceration indexes for 5 types of experimental ulcers. In each test, the test compounds were suspended in a 0.5% aqueous solution of carboxymethyl cellulose and administered orally in a series of appropriately selected doses ranging from 1 to 100 mg/kg. The test procedures for 5 types of experimental ulcers were as follows:

(Shay's ulcer)

In rats which had been fasted for 48 hours, the pyloric end of the stomach was ligated and they were maintained for 14 hours without giving any food or water. Then, each rat was sacrificed and the area of the ulcer(s) formed in the forestomach part was measured. The ulceration index was calculated on the basis of the data thus obtained. The test compounds were administered 30 minutes before ligation.

(Water-immersion stress ulcer)

Rats which had been fasted for 15 hours were immobilized in stress cages and immersed chest-deep in a water bath at 21°C. After 10 hours, each rat was sacrificed and the length of the ulcer(s) formed in the glandular stomach part was measured. The ulceration index was calculated on the basis of the data thus obtained. The test compounds were administered 10 minutes before exposure to the stress.

(Hydrochloric acid-ethanol ulcer)

To rats which had been fasted for 24 hours, a 150 mM hydrochloric acid-60% ethanol mixture was orally administered in an amount of 0.5 ml per 100 g of body weight. After an hour, each rat was sacrificed and the length of the ulcer(s) formed in the glandular stomach part was measured. The ulceration index was calculated on the basis of the data thus obtained. The test compounds were administered 30 minutes before administration of the hydrochloric acid-ethanol mixture.

(Indomethacin ulcer)

To rats which had been fasted for 24 hours, indomethacin was subcutaneously administered in a dose of 25 mg/kg. After 7 hours, each rat was sacrificed and the length of the ulcer(s) formed in the glandular stomach part was measured. The ulceration index was calculated on the basis of the data thus obtained. The test compounds were administered 30 minutes before administration of indomethacin.

(Aspirin ulcer)

In rats which had been fasted for 24 hours, the pyloric end of the stomach was ligated. After 5 minutes, aspirin was orally administered thereto in a dose of 150 mg/kg. Seven hours after ligation, each rat was sacrificed and the length of the ulcer(s) formed in the glandular stomach part was measured. The ulceration index was calculated on the basis of the data thus obtained. The test compounds were administered 30 minutes before ligation.

The pharmacological effect of the test compounds on each of the aforesaid experimental ulcers was evaluated on the basis of the dose (in mg/kg) required to inhibit the formation of ulcers by 50% (hereinafter referred to as ID_{50}). The ID_{50} value of each test compound was determined by calculatin the difference in ulceration index between the untreated group and each treated group, dividing the difference by the ulceration index of the untreated group to obtain the degree of inhibition, and constructing a dose-response curve on the basis of the data thus obtained. The results are shown in Table 4. For purposes of comparison, the ID_{50} values of Omeprazole and Compounds α and β were determined in the same manner as described above and are also shown in Table 4.

Table 4

Test compound / Experimental ulcer	Inhibitory effects on various experimental ulcers, ID_{50} (mg/kg)			
	Omeprazole	Compound α	Compound β	Example 1
Shay's ulcer	30.3	100 or greater	42.0	11.0
Water-immersion stress ulcer	39.7	100 or greater	63.3	26.4
Hydrochloric acid-ethanol ulcer	13.6	63.3	25.4	5.1
Indomethacin ulcer	24.7	78.4	29.5	12.9
Aspirin ulcer	17.2	100 or greater	23.8	6.3

Test compound / Experimental ulcer	Inhibitory effects on various experimental ulcers, ID_{50} (mg/kg)				
	Example 8	Example 13	Example 24	Example 26	Example 33
Shay's ulcer	15.1	17.4	10.8	14.7	19.2
Water-immersion stress ulcer	34.2	37.3	27.0	30.5	35.1
Hydrochloric acid-ethanol ulcer	8.2	9.6	3.5	7.9	10.3
Indomethacin ulcer	18.8	21.9	13.1	15.8	23.2
Aspirin ulcer	10.7	14.5	5.4	9.5	12.6

As is evident from Table 4, it can be recognized that the present compounds [I] have a very good inhibitory effect on various types of ulcers.

(v) Toxicity test

The acute toxicity (LD_{50}) of several typical examples of the present compounds [I] (i.e., the compounds of Examples 1, 8, 13, 19, 24, 26 and 33) was tested with 5-weeks-old male Wistar rats. The LD_{50} values of all compounds were greater than 4000 mg/kg in the case of oral administration, and greater than 500 mg/kg in the case of intraperitoneal administration. When Omeprazole was administered orally, its LD_{50} value was greater than 4000 mg/kg.

In consideration of the results of the above-described tests, the present compounds [I] may be said to be potent drugs useful for the treatment of gastric and duodenal ulcers and scarcely susceptible to inactivation during storage.

The present compounds [I] can be admixed with conventional pharmaceutical carriers to form various types of pharmaceutical compositions including solid preparations such as tablets, capsules, granules, powders, fine granules, etc., and liquid preparations such as injectable solutions, syrups, elixirs, suspensions, emulsions, etc. Solid preparations may be coated so as to provide them with enteric coatings. Liquid preparations may be made by reacting one of the present compounds [I] with an alkali to form a physiologically acceptable salt thereof and then dissolving this salt in water, or by dissolving one of the present compounds [I] in an aqueous solution of an alkali. The pharmaceutical carriers used for these purposes may be selected according to the desired dosage form. Examples of the pharmaceutical carriers include excipients, binders and disintegrants, such as corn starch, dextrin, α-, β- or γ-cyclodextrin, glucose, lactose, sucrose, methylcellulose, ethylcellulose, calcium carboxymethylcellulose, crystalline cellulose, magnesium stearate, sodium alginate, Witepsol W35, Witepsol E85, polyvinyl alcohol, synthetic aluminum silicate, etc.; lubricants and coating agents such as talc, waxes, hydroxypropyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl methylcellulose, cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate, polyvinyl alcohol phthalate, styrene-maleic anhydride copolymer, polyvinyl acetal diethylaminoacetate, etc.; solubilizing agents such as glycerol, propylene glycol, mannitol, etc.; emulsifying or suspending agents such as polyoxyethylene stearate, polyoxyethylene cetyl alcohol ether, polyethylene glycol, polyvinyl pyrrolidone, etc.; stabilizers such as sorbitol, Tween 80, Span 60, fats and oils, etc.; and various solvents.

The dosage level of the present compounds [I] varies with the age of the patient, the severity of the disease, and the like. However, they are usually used in a daily dose of 0.5 to 2000 mg, preferably 3 to 200 mg, for adults. This daily dose may be administered in one to six divided doses, preferably in one to three divided doses.

The present invention is further illustrated by the following Reference Examples and Examples. The Reference Examples illustrates the preparation of sulfide compounds [II].

Reference Example A

1.81 g (0.01 mole) of 2-mercapto-5-methoxyimidazo-[4,5-b]pyridine and 1.92 g (0.01 mole) of 2-chloromethyl-3,5-dimethylpyridine hydrochloride were added to 100 ml of ethanol containing 1.12 g (0.02 mole) of potassium hydroxide, and this mixture was heated under reflux for 2 hours. Upon cooling to room temperature, the resulting reaction solution was filtered to remove any insoluble matter, and the filtrate was concentrated under reduced pressure. The resulting residue was dissolved in 500 ml of chloroform, and this solution was washed with water, dried over anhydrous sodium sulfate and then evaporated to dryness under reduced pressure. The resulting residue was subjected to silica gel column chromatography using chloroform as the developing solvent. Thus, there was obtained 2.20 g (73.3% yield) of 2-[2-(3,5-dimethyl)-pyridylmethylthio-5-methoxyimidazo[4,5-b]pyridine in the form of colorless crystals having a melting point of 175-176°C.

The following 24 compounds were prepared in substantially the same manner as described above, except that the 2-mercapto-5-methoxyimidazo[4,5-b]pyridine was replaced by 0.01 mole of each of the corresponding thiol compounds [III] and the 2-chloromethyl-3,5-dimethylpyridine hydrocholoride was replaced by 0.01 mole of each of the corresponding pyridine compounds [IV].

2-[2-(3,5-Dimethyl-4-methoxy)pyridylmethylthio]-5-methoxyimidazo[4,5-b]pyridine, m.p. 154-155°C.
2-[2-(3,4,5-Trimethyl)pyridylmethylthio]-5-methoxyimidazo[4,5-b]pyridine, m.p. 150-151°C.
2-[2-(4-Methoxy-5-methyl)pyridylmethylthio]-5-methoxyimidazo[4,5-b]pyridine, m.p. 160-162°C.
2-[2-(4-Methyl)pyridylmethylthio]-5-methoxyimidazo-[4,5-b]pyridine, m.p. 134-137°C.
2-[2-(3,5-Dimethyl)pyridylmethylthio]-6-methoxyimidazo[4,5-b]pyridine, glassy material.
2-[2-(4-Methoxy-5-methyl)pyridylmethylthio]-7-methoxyimidazo[4,5-b]pyridine, glassy material.
2-[2-(3,4,5-Trimethyl)pyridylmethylthio]-5-ethoxyimidazo[4,5-b]pyridine, m.p. 127-128°C.
2-[2-(3,4,5-Trimethyl)pyridylmethylthio]-7-ethoxyimidazo[4,5-b]pyridine, m.p. 132-136°C.
2-[2-(3,5-Dimethyl)pyridylmethylthio]-5-isopropyloxyimidazo[4,5-b]pyridine, m.p. 159-160°C.
2-[2-(4-Methyl)pyridylmethylthio]-5-sec-butyloxyimidazo[4,5-b]pyridine, glassy material.
2-[2-(3,4,5-Trimethyl)pyridylmethylthio-5-n-butyloxyimidazo[4,5-b]pyridine, m.p. 119-120°C.
2-[2-(4-Methoxy-5-methyl)pyridylmethylthio]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine, m.p. 159-161°C.
2-[2-(3,5-Dimethyl)pyridylmethylthio]-5-ethoxyimidazo[4,5-b]pyridine, m.p. 146-147°C.
2-[2-(3,5-Dimethyl-4-methoxy)pyridylmethylthio]-5-isopropyloxyimidazo[4,5-b]pyridine, m.p. 130-133°C.
2-[2-(4-Methoxy-5-methyl)pyridylmethylthio]-5-isopropyloxyimidazo[4,5-b]pyridine, m.p. 92-94°C.
2-[2-(4-Methoxy)pyridylmethylthio]-5-isopropyloxyimidazo[4,5-b]pyridine, m.p. 134-136°C.
2-[2-(3,5-Dimethyl)pyridylmethylthio]-5-n-propyloxyimidazo[4,5-b]pyridine, m.p. 116-117°C.
2-[2-(3,5-Dimethyl)pyridylmethylthio]-5-isobutyloxyimidazo[4,5-b]pyridine, m.p. 139-141°C.

2-[2-(3,5-Dimethyl-4-methoxy)pyridylmethylthio]-5-isobutyloxyimidazo[4,5-b]pyridine, m.p. 132-135°C.
2-[2-(4-Methoxy-5-methyl)pyridylmethylthio]-5-isobutyloxyimidazo[4,5-b]pyridine, m.p. 153-154°C.
2-[2-(4-Methoxy)pyridylmethylthio]-5-isobutyloxyimidazo[4,5-b]pyridine, m.p. 119-122°C.
2-[2-(3,5-Dimethyl)pyridylmethylthio]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine, m.p. 126-128°C.
2-[2-(3,5-Dimethyl-4-methoxy)pyridylmethylthio]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine, m.p. 150-153°C.
2-[2-(4-Methoxy)pyridylmethylthio]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine, m.p. 115-117°C.

Reference Example B

2.50 g (0.01 mole) of 2-mercapto-5-(2,2,2-trifluoroethoxy)imidazo[4,5-b]pyridine and 2.22 g (0.01 mole) of 2-chloromethyl-4-methoxy-3,5-dimethylpyridine hydrochloride were added to 100 ml of ethanol, and this mixture was stirred at 60°C for 2 hours. After the resulting reaction solution was concentrated under reduced pressure, 150 ml of a saturated aqueous solution of sodium hydrogen carbonate was added to the residue. This mixture was stirred and then extracted with 300 ml of chloroform. The extract thus obtained was dried over anhydrous sodium sulfate and then evaporated to dryness under reduced pressure. The desired product was isolated and purified by subjecting the resulting residue to silica gel column chromatography using a 50:1 mixture of chloroform and ethanol as the developing solvent. Thus, there was obtained 3.25 g (81.5% yield) of 2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylthio]-5-(2,2,2-trifluoroethoxy)-imidazo[4,5-b]pyridine in the form of colorless crystals having a melting point of 178-180°C.

The following 11 compounds were prepared in substantially the same manner as described above, except that the 2-mercapto-5-(2,2,2-trifluoroethoxy)imidazo[4,5-b]pyridine was replaced by 0.01 mole of each of the corresponding thiol compounds [III] and the 2-chloromethyl-4-methoxy-3,5-dimethylpyridine hydrochloride was replaced by 0.01 mole of each of the corresponding pyridine compounds [IV].
2-[2-(3,5-Dimethyl)pyridylmethylthio]-5-(2,2,2-trifluoroethoxy)imidazo[4,5-b]pyridine, m.p. 173-174°C.
2-[2-(3,4,5-Trimethyl)pyridylmethylthio]-6-(2,2,2-trifluoroethoxy)imidazo[4,5-b]pyridine, m.p. 145-148°C.
2-[2-(4-Methoxy-5-methyl)pyridylmethylthio]-7-(2,2,2-trifluoroethoxy)imidazo[4,5-b]pyridine, m.p. 157-159°C.
2-[2-(4-Methyl)pyridylmethylthio]-5-(2,2,3,3,4,4,4-heptafluorobutyloxy)imidazo[4,5-b]pyridine, glassy material.
2-[2-(3,5-Dimethyl)pyridylmethylthio]-5-n-pentyloxyimidazo[4,5-b]pyridine, m.p. 101-103°C.
2-[2-(3,4,5-Trimethyl)pyridylmethylthio]-6-n-hexyloxyimidazo[4,5-b]pyridine, m.p. 96-99°C.
2-[2-(3,5-Dimethyl)pyridylmethylthio]-5-n-heptyloxyimidazo[4,5-b]pyridine, m.p. 119-120°C.
2-[2-(3,5-Dimethyl)pyridylmethylthio]-5-(3-methylbutyloxy)imidazo[4,5-b]pyridine, m.p. 101-104°C.
2-[2-(4-Methoxy-5-methyl)pyridylmethylthio]-7-(2,4,4-trimethylpentyloxy)imidazo[4,5-b]pyridine, glassy material.
2-[2-(3,5-Dimethyl-4-methoxy)pyridylmethylthio]-6-(3- cyclopentylpropyloxy)imidazo[4,5-b]pyridine, glassy material.
2-[2-(4-Methyl)pyridylmethylthio]-7-cyclohexylmethyloxyimidazo[4,5-b]pyridine, glassy material.

Example 1

1.50 g (0.005 mole) of 2-[2-(3,5-dimethyl)pyridylmethylthio]-5-methoxyimidazo[4,5-b]pyridine was dissolved in 150 ml of chloroform. To this solution was slowly added 0.86 g (0.005 mole) of m-chloroperbenzoic acid at 0-5°C, followed by stirring at that temperature for 10 minutes. While the resulting reaction solution was being kept at 0-5°C, 30 ml of a 5% aqueous solution of sodium hydrogen carbonate was injected thereinto and mixed therewith. Thereafter, the chloroform layer was separated, dried over anhydrous sodium sulfate, and then evaporated to dryness under reduced pressure. The resulting residue was recrystallized from ethyl acetate to obtain 1.18 g (74.7% yield) of 2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine in the form of colorless crystals. This product had a melting point of 175-177°C.

Infrared absorption spectrum (KBr, cm^{-1}): 1060(S=O).

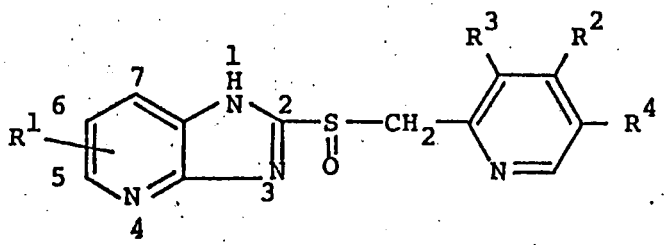
Analysis:

Calcd. for $C_{15}H_{16}N_4O_2S$ (%) C, 56.94; H, 5.10; N, 17.71
Found (%) C, 57.03; H, 5.04; N, 17.82

Examples 2-37

The compounds listed in Table 5 were prepared in substantially the same manner as described in Example 1, except that the 2-[2-(3,5-dimethyl)pyridylmethylthio]-5-methoxyimidazo[4,5-b]pyridine (0.005 mole) was replaced by each of the corresponding sulfide compounds [II] (0.005 mole), and the reaction temperature and the reaction time were suitably modified. These compounds were obtained in a yield ranging from 72.4% to 90.8%.

Table 5



Example No.	R^1	R^2	R^3	R^4	Melting point °C (Recrystn. solvent)	IR (KBr) cm^{-1}	Elemental analysis Molecular formula: upper row Calcd. (%) lower row Found (%)
2	5-OCH_3	OCH_3	CH_3	CH_3	174 - 175 (ethyl ether)	1030 (S=O)	$C_{16}H_{18}N_4O_3S$: C,55.47 H,5.24 N,16.18 C,55.62 H,5.37 N,16.07
3	5-OCH_3	CH_3	CH_3	CH_3	188 - 190 (acetonitrile-chloroform)	1050 (S=O)	$C_{16}H_{18}N_4O_2S$: C,58.16 H,5.49 N,16.96 C,58.36 H,5.55 N,16.75
4	5-OCH_3	OCH_3	H	CH_3	180 - 184 (ethyl acetate)	1030 (S=O)	$C_{15}H_{16}N_4O_3S$: C,54.20 H,4.85 N,16.86 C,54.12 H,4.96 N,16.68
5	5-OCH_3	CH_3	H	H	139 - 141 (ethyl acetate)	1050 (S=O)	$C_{14}H_{14}N_4O_2S$: C,55.61 H,4.67 N,18.53 C,55.79 H,4.78 N,18.48

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Table 5 (continued)

Example No.	R^1	R^2	R^3	R^4	Melting point °C (Recrystn. solvent)	IR (KBr) cm^{-1}	Elemental analysis Molecular formula: upper row Calcd. (%) lower row Found (%)
6	6-OCH_3	H	CH_3	CH_3	163 - 166 (ethyl acetate)	1050 (S=O)	$C_{15}H_{16}N_4O_2S$: C,56.94 H,5.10 N,17.71 C,56.76 H,5.25 N,17.59
7	7-OCH_3	OCH_3	H	CH_3	175 - 178 (ethyl acetate)	1050 (S=O)	$C_{15}H_{16}N_4O_3S$: C,54.20 H,4.85 N,16.86 C,54.01 H,4.92 N,16.82
8	5-OC_2H_5	CH_3	CH_3	CH_3	160 - 163 (ethyl acetate)	1050 (S=O)	$C_{17}H_{20}N_4O_2S$: C,59.28 H,5.85 N,16.27 C,59.35 H,5.92 N,16.21
9	7-OC_2H_5	CH_3	CH_3	CH_3	165 - 167 (ethyl acetate)	1050 (S=O)	$C_{17}H_{20}N_4O_2S$: C,59.28 H,5.85 N,16.27 C,59.48 H,5.89 N,16.38
10	5-$OCH(CH_3)_2$	H	CH_3	CH_3	146 - 148 (methanol-ethyl ether)	1040 (S=O)	$C_{17}H_{20}N_4O_2S$: C,59.28 H,5.85 N,16.27 C,59.49 H,5.80 N,16.27

Table 5 (continued)

Example No.	R^1	R^2	R^3	R^4	Melting point °C (Recrystn. solvent)	IR (KBr) cm^{-1}	Elemental analysis Molecular formula: upper row Calcd. (%) lower row Found (%)
11	5-OCHCH$_2$CH$_3$ (CH$_3$)	CH_3	H	H	glassy material (ethyl ether)	1040 (S=O)	$C_{17}H_{20}N_4O_2S$: C,59.28 H,5.85 N,16.27 C,59.20 H,5.97 N,16.48
12	5-O-n-C_4H_9	CH_3	CH_3	CH_3	glassy material (ethyl ether)	1040 (S=O)	$C_{19}H_{24}N_4O_2S$: C,61.26 H,6.49 N,15.04 C,61.54 H,6.51 N,15.11
13	5-OCH$_2$-cyclopropyl	OCH_3	H	CH_3	154 - 157 (methanol-ethyl ether)	1050 (S=O)	$C_{18}H_{20}N_4O_3S$: C,58.04 H,5.41 N,15.05 C,58.02 H,5.29 N,14.92
14	5-OC_2H_5	H	CH_3	CH_3	151 - 152 (ethyl acetate)	1060 (S=O)	$C_{16}H_{18}N_4O_2S$: C,58.16 H,5.49 N,16.96 C,58.42 H,5.53 N,16.98
15	5-OCH(CH$_3$)$_2$	OCH_3	CH_3	CH_3	124 - 126 (chloroform-ethyl ether)	1060 1080 (S=O)	$C_{18}H_{22}N_4O_3S$: C,57.74 H,5.92 N,14.96 C,57.96 H,5.99 N,14.81

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Table 5 (continued)

Example No.	R^1	R^2	R^3	R^4	Melting point °C (Recrystn. solvent)	IR (KBr) cm^{-1}	Elemental analysis Molecular formula: upper row Calcd. (%) lower row Found (%)
16	5-OCH(CH$_3$)$_2$	OCH_3	H	CH_3	169 - 173 (chloroform-ethyl ether)	1040 (S=O)	$C_{17}H_{20}N_4O_3S$: C,56.65 H,5.59 N,15.54 C,56.54 H,5.45 N,15.60
17	5-OCH(CH$_3$)$_2$	OCH_3	H	H	150 - 152 (chloroform-ethyl ether)	1060 (S=O)	$C_{16}H_{18}N_4O_3S$: C,55.48 H,5.24 N,16.17 C,55.55 H,5.37 N,16.27
18	5-$OCH_2CH_2CH_3$	H	CH_3	CH_3	163 - 166 (ethyl acetate)	1060 (S=O)	$C_{17}H_{20}N_4O_2S$: C,59.28 H,5.85 N,16.27 C,59.32 H,5.87 N,16.40
19	5-OCH_2CH(CH$_3$)$_2$	H	CH_3	CH_3	150 - 151 (ethyl acetate-hexane)	1060 (S=O)	$C_{18}H_{22}N_4O_2S$: C,60.31 H,6.19 N,15.63 C,60.43 H,6.25 N,15.82
20	5-OCH_2CH(CH$_3$)$_2$	OCH_3	CH_3	CH_3	160 - 161 (ethyl ether)	1080 (S=O)	$C_{19}H_{24}N_4O_3S$: C,58.74 H,6.23 N,14.42 C,58.55 H,6.40 N,14.21

Table 5 (continued)

Example No.	R^1	R^2	R^3	R^4	Melting point °C (Recrystn. solvent)	IR (KBr) cm^{-1}	Elemental analysis Molecular formula: upper row Calcd. (%) lower row Found (%)
21	5-$OCH_2CH(CH_3)_2$	OCH_3	H	CH_3	142 - 144 (ethyl ether)	1080 (S=O)	$C_{18}H_{22}N_4O_3S$: C,57.74 H,5.92 N,14.96 C,57.97 H,6.03 N,14.99
22	5-$OCH_2CH(CH_3)_2$	OCH_3	H	H	157 - 159 (ethyl ether)	1050 (S=O)	$C_{17}H_{20}N_4O_3S$: C,56.65 H,5.59 N,15.54 C,56.90 H,5.84 N,15.47
23	5-OCH_2-cyclopropyl	H	CH_3	CH_3	155 - 157 (chloroform-ethyl ether)	1060 (S=O)	$C_{18}H_{20}N_4O_2S$: C,60.65 H,5.66 N,15.72 C,60.82 H,5.75 N,15.59
24	5-OCH_2-cyclopropyl	OCH_3	CH_3	CH_3	150 - 154 (ethyl acetate)	1060 1080 (S=O)	$C_{19}H_{22}N_4O_3S$: C,59.05 H,5.74 N,14.50 C,59.19 H,5.90 N,14.43
25	5-OCH_2-cyclopropyl	OCH_3	H	H	149 - 151 (ethyl acetate)	1040 (S=O)	$C_{17}H_{18}N_4O_3S$: C,56.97 H,5.06 N,15.63 C,57.20 H,5.21 N,15.62

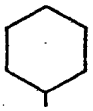
Table 5 (continued)

Example No.	R^1	R^2	R^3	R^4	Melting point °C (Recrystn. solvent)	IR. (KBr) cm^{-1}	Elemental analysis Molecular formula: upper row Calcd. (%) lower row Found (%)
26	5-OCH_2CF_3	OCH_3	CH_3	CH_3	169 - 170 (ethyl acetate)	1060 1080 (S=O).	$C_{17}H_{17}N_4O_3SF_3$: C,49.27 H,4.13 N,13.52 C,49.25 H,4.20 N,13.56
27	5-OCH_2CF_3	H	CH_3	CH_3	172 - 174 (ethyl acetate)	1070 (S=O)	$C_{16}H_{15}N_4O_2SF_3$: C,50.00 H,3.93 N,14.58 C,50.21 H,4.01 N,14.51
28	6-OCH_2CF_3	CH_3	CH_3	CH_3	165 - 168 (ethyl acetate)	1060 (S=O)	$C_{17}H_{17}N_4O_2SF_3$: C,51.25 H,4.30 N,14.06 C,51.40 H,4.37 N,14.13
29	7-OCH_2CF_3	OCH_3	H	CH_3	159 - 162 (ethyl acetate)	1060 (S=O)	$C_{16}H_{15}N_4O_3SF_3$: C,48.00 H,3.78 N,13.99 C,48.09 H,3.73 N,13.87
30	5-$OCH_2(CF_2)_2CF_3$	CH_3	H	H	colorless glassy material (ethyl ether)	1070 (S=O)	$C_{17}H_{13}N_4O_2SF_7$: C,43.41 H,2.79 N,11.91 C,43.54 H,2.91 N,11.88

Table 5 (continued)

Example No.	R^1	R^2	R^3	R^4	Melting point °C (Recrystn. solvent)	IR (KBr) cm^{-1}	Elemental analysis Molecular formula: upper row Calcd. (%) lower row Found (%)
31	5-O$(CH_2)_4CH_3$	H	CH_3	CH_3	119 - 122 (dichloromethane-ethyl ether)	1060 (S=O)	$C_{19}H_{24}N_4O_2S$: C,61.27 H,6.49 N,15.04 C,61.07 H,6.63 N,15.21
32	6-O$(CH_2)_5CH_3$	CH_3	CH_3	CH_3	125 - 127 (dichloromethane)	1060 (S=O)	$C_{21}H_{28}N_4O_2S$: C,62.97 H,7.05 N,13.99 C,62.78 H,7.01 N,14.12
33	5-O$(CH_2)_6CH_3$	H	CH_3	CH_3	126 - 127 (ethyl acetate)	1070 (S=O)	$C_{21}H_{28}N_4O_2S$: C,62.97 H,7.05 N,13.99 C,63.20 H,6.99 N,13.83
34	5-O$(CH_2)_2$-CH(CH_3)(CH_3)	H	CH_3	CH_3	115 - 120 (ethyl ether)	1070 (S=O)	$C_{19}H_{24}N_4O_2S$: C,61.27 H,6.49 N,15.04 C,61.33 H,6.62 N,15.17
35	7-OCH_2-CH(CH_3)-CH_2-C(CH_3)(CH_3)	OCH_3	H	CH_3	colorless glassy material (ethyl ether)	1060 (S=O)	$C_{22}H_{30}N_4O_3S$: C,61.37 H,7.02 N,13.01 C,61.51 H,7.26 N,12.95

Table 5 (continued)

Example No.	R^1	R^2	R^3	R^4	Melting point °C (Recrystn. solvent)	IR (KBr) cm^{-1}	Elemental analysis Molecular formula: upper row Calcd. (%) lower row Found (%)
36	6-O$(CH_2)_3$- 	OCH_3	CH_3	CH_3	colorless glassy material (ethyl ether)	1070 (S=O)	$C_{23}H_{30}N_4O_3S$: C,62.42 H,6.83 N,12.66 C,62.19 H,6.75 N,12.78
37	7-OCH_2- 	CH_3	H	H	colorless glassy material (ethyl ether)	1070 (S=O)	$C_{20}H_{24}N_4O_2S$: C,62.48 H,6.29 N,14.57 C,62.64 H,6.17 N,14.34

Now, the preparation of several pharmaceutical compositions containing the present compounds [I] will be described hereinbelow.

(Tablets)

		% by weight
(1)	Compound of Example 1	25.0
(2)	Lactose	41.0
(3)	Corn starch	15.0
(4)	Crystalline cellulose	15.0
(5)	Hydroxypropyl cellulose	3.0
(6)	Magnesium stearate	1.0
		100.0

The above ingredients (1)-(5) were blended together. After the addition of water, the resulting mixture was granulated and then dried. The granules so formed were adjusted to a predetermined size range, and the ingredient (6) was added thereto. The resulting mixture was compressed to form tablets each containing 100 mg of the active ingredient.

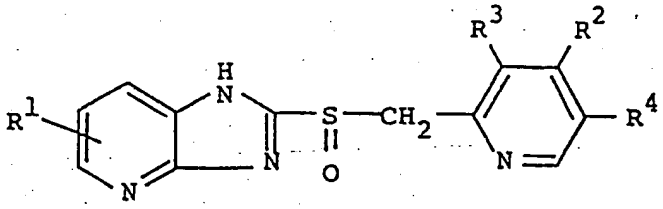
(Capsules)

		% by weight
(1)	Compound of Example 24	25.0
(2)	Lactose	50.0
(3)	Corn starch	20.0
(4)	Hydroxypropyl cellulose	3.0
(5)	Synthetic aluminum silicate	1.0
(6)	Magnesium stearate	1.0
		100.0

According to conventional procedure, the above ingredients were blended together and then granulated. The granules so formed were filled into capsules, each of which contained 100 mg of the active ingredient.

Claims

1. An imidazo[4,5-b]pyridine compound of the general formula

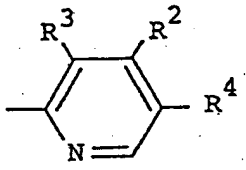


where R^1 is a straight-chain or branched alkoxy group of 1 to 8 carbon atoms (which may be substituted with a cycloalkyl group) or a fluoroalkyloxy group of 2 to 4 carbon atoms, R^2 is a hydrogen atom, a methyl group or a methoxy group, and R^3 and R^4 are each a hydrogen atom or a methyl group and may be the same or different.

2. A compound as claimed in claim 1 wherein the straight-chain or branched alkoxy group is selected from the group consisting of methoxy, ethoxy, isopropyloxy, n-propyloxy, sec-butyloxy, isobutyloxy, n-butyloxy, n-pentyloxy, 3-methylbutyloxy, n-hexyloxy, n-heptyloxy, 2,4,4-trimethylpentyloxy, cyclopropylmethyloxy, 3-cyclopentylpropyloxy and cyclohexylmethyloxy, or the fluoroalkyloxy group is selected

from the group consisting of 2,2,2-trifluoroethoxy and 2,2,3,3,4,4,4-heptafluorobutyloxy.

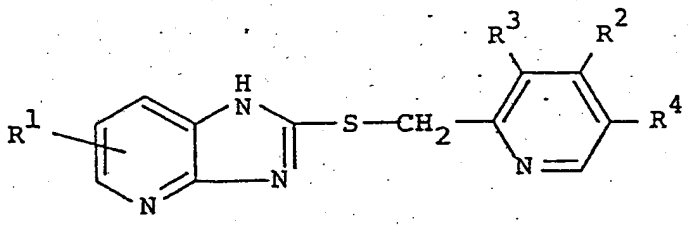
3. A compound as claimed in either of claims 1 and 2 wherein the substituted pyridyl group represented by the general formula



is selected from the group consisting of 2-(3,5-dimethyl)pyridyl, 2-(3,5-dimethyl-4-methoxy)pyridyl, 2-(3,4,5-trimethyl)pyridyl, 2-(4-methoxy-5-methyl)pyridyl, 2-(4-methoxy)pyridyl and 2-(4-methyl)pyridyl.

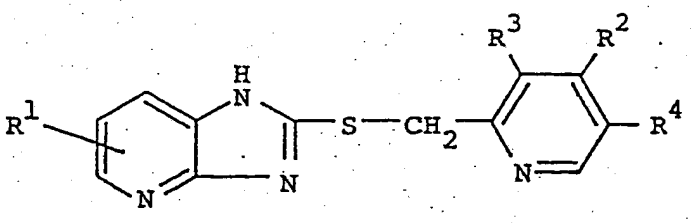
4. A compound as claimed in claim 1 which is any one of the following compounds,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-7-methoxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylsulfinyl]-5-ethoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylsulfinyl]-5-n-butyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-ethoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-n-propyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy)pyridylmethylsulfinyl]-5-isobutyloxy imidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-cyclopropylmethoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-(2,2,2-trifluoroethoxy)imidazo[4,5-b]pyridine,
2-[2-(4-methyl)pyridylmethylsulfinyl]-5-(2,2,3,3,4,4,4-heptafluorobutyloxy)imidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-n-heptyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-(3-methylbutyloxy)imidazo[4,5-b]pyridine or
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-6-(3-cyclopentylpropyloxy)imidazo[4,5-b]pyridine.

5. A process for preparing an imidazo[4,5-b]pyridine compound of claim 1 wherein a sulfide compound of the general formula



where R^1, R^2, R^3 and R^4 are as defined in claim 1 is oxidised in the presence of a solvent and with the aid of an oxidising agent.

6. A sulfide compound of the general formula



where R^1 is a straight-chain or branched alkoxy group of 1 to 8 carbon atoms (which may be substituted with a cycloalkyl group) or a fluoroalkyloxy group of 2 to 4 carbon atoms, R^2 is a hydrogen atom, a methyl group or a methoxy group, and R^3 and R^4 are each a hydrogen atom or a methyl group and may be the same or different.

7. A compound as claimed in claim 6 which is any one of the following compounds,
2-[2-(3,5-dimethyl)pyridylmethylthio]-5-methoxy imidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylthio]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylthio]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylthio]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(4-methyl)pyridylmethylthio]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylthio]-6-methoxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylthio]-7-methoxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylthio]-5-ethoxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylthio]-7-ethoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylthio]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methyl)pyridylmethylthio]-5-sec-butyloxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylthio]-5-n-butyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylthio]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylthio]-5-ethoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylthio]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylthio]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy)pyridylmethylthio]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylthio]-5-n-propyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylthio]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylthio]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylthio]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy)pyridylmethylthio]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylthio]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylthio]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy)pyridylmethylthio]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylthio]-5-(2,2,2-trifluoroethoxy)imidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylthio]-5-(2,2,2-trifluoroethoxy)imidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylthio]-6-(2,2,2-trifluoroethoxy)imidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylthio]-7-(2,2,2-trifluoroethoxy)imidazo[4,5-b]pyridine,
2-[2-(4-methyl)pyridylmethylthio]-5-(2,2,3,3,4,4,4-heptafluorobutyloxy)imidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylthio]-5-n-pentyloxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylthio]-6-n-hexyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylthio]-5-n-heptyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylthio]-5-(3-methylbutyloxy)imidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylthio]-7-(2,4,4-trimethylpentyloxy)imidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylthio]-6-(3-cyclopentylpropyloxy)imidazo[4,5-b]pyridine or
2-[2-(4-methyl)pyridylmethylthio]-7-cyclohexylmethyloxyimidazo[4,5-b]pyridine.

8. A pharmaceutical composition comprising an imidazo[4,5-b]pyridine compound of claim 1.

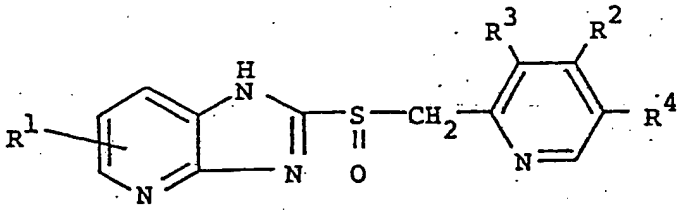
9. A pharmaceutical composition as claimed in claim 8 where the imidazo[4,5-b]pyridine compound of claim 1 is selected from the group consisting of
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-7-methoxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylsulfinyl]-5-ethoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylsulfinyl]-5-n-butyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-ethoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-n-propyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5- isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,

2-[2-(4-methoxy)pyridylmethylsulfinyl-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-(2,2,2-trifluoroethoxy)imidazo[4,5-b]pyridine,
2-[2-(4-methyl)pyridylmethylsulfinyl]-5-(2,2,3,3,4,4,4-heptafluorobutyloxy)imidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-n-heptyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-(3-methylbutyloxy)imidazo[4,5-b]pyridine and
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-6-(3-cyclopentylpropyloxy)imidazo[4,5-b]pyridine.

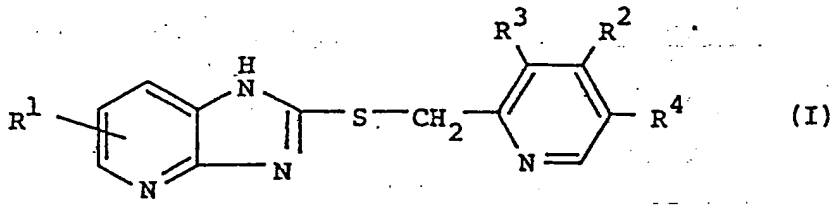
10. The use of a compound as claimed in any of claims 1 to 4 for the manufacture of a medicament for the treatment of gastric and/or duodenal ulcers.

Claims for the following contracting states: Spain, Austria and Greece

1. A process for preparing an imidazo[4,5-b]pyridine compound of the general formula



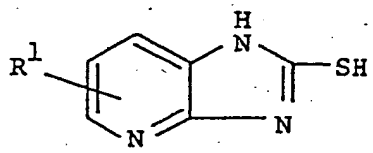
where R^1 is a straight-chain or branched alkoxy group of 1 to 8 carbon atoms (which may be substituted with a cycloalkyl group) or a fluoroalkyloxy group of 2 to 4 carbon atoms, R^2 is a hydrogen atom, a methyl group or a methoxy group, and R^3 and R^4 are each a hydrogen atom or a methyl group and may be the same or different, wherein a sulfide compound of the general formula (I)



(I)

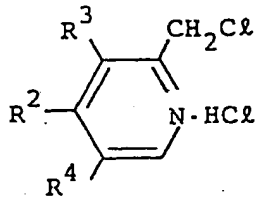
(where R^1, R^2, R^3 and R^4 are as previously defined) is oxidised in the presence of a solvent and with the aid of an oxidizing agent.

2. A process as claimed in claim 1 wherein the compound of formula (I) is obtained by condensing a thiol compound of general formula (II)



(II)

(wherein R^1 is as defined in claim 1) with a pyridine compound of general formula (III)



(III)

(wherein R^2, R^3 and R^4 are as defined in claim 1) in a solvent, optionally in the presence of a base.

3. A process as claimed in claim 2 wherein the pyridine compound of formula (III) is used in an amount equimolar to the thiol compound of formula (II) and, if present, the base is used in an amount of 2.0 to 3.0 moles per mole of the thiol compound, the condensation reaction being carried out at a temperature of from 10 to 200° C for a period of from 1 minute to 12 hours; and thereafter the oxidizing agent is used in a amount of 1.0 to 1.3 moles per mole of the sulfide compound obtained, and the oxidation reaction is carried out at a temperature of from -70 to 30° C for a period of from 1 minute to 24 hours.

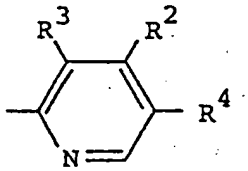
4. A process as claimed in claim 2 or claim 3 where the solvent for the condensation step is selected from the group consisting of methanol, ethanol, propanol, butanol, dimethylformamide, dimethyl sulfoxide, water and mixtures of two or more such solvents, and the solvent for the oxidation step is selected from the group consisting of chloroform, tetrachloroethane, methanol, ethanol, butanol and mixtures of two or more such solvents.

5. A process as claimed in any of claims 2 to 4 where the base is selected from the group consisting of sodium hydrogen carbonate, sodium carbonate, potassium carbonate, sodium hydroxide and potassium hydroxide.

6. A process as claimed in any preceding claim where the oxidizing agent is selected from the group consisting of m-chloroperbenzoic acid, perbenzoic acid and peracetic acid.

7. A process as claimed in claim 1 where the straight-chain or branched alkoxy group is selected from the group consisting of methoxy, ethoxy, isopropyloxy, n-propyloxy, sec-butyloxy, isobutyloxy, n-butyloxy, n-pentyloxy, 3-methylbutyloxy, n-hexyloxy, n-heptyloxy, 2,4,4-trimethylpentyloxy, cyclopropylmethyloxy, 3-cyclopentylpropyloxy and cyclohexylmethyloxy, or the fluoroalkyloxy group is selected from the group consisting of 2,2,2-trifluoroethoxy and 2,2,3,3,4,4,4-heptafluorobutyloxy.

8. A process as claimed in claim 1 where the substituted pyridyl group represented by the general formula



is selected from the group consisting of 2-(3,5-dimethyl)pyridyl, 2-(3,5-dimethyl-4-methoxy)pyridyl, 2-(3,4,5-trimethyl)pyridyl, 2-(4-methoxy-5-methyl)pyridyl, 2-(4-methoxy)pyridyl and 2-(4-methyl)pyridyl.

9. A process as claimed in claim 1 where the imidazo[4,5-b]pyridine compound is selected from the group consisting of
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-7-methoxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylsulfinyl]-5- ethoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylsulfinyl]-5-n-butyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-ethoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-n-propyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-(2,2,2-trifluoroethoxy)imidazo[4,5-b]pyridine,
2-[2-(4-methyl)pyridylmethylsulfinyl]-5-(2,2,3,3,4,4,4-heptafluorobutyloxy)imidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-n-heptyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-(3-methylbutyloxy)imidazo[4,5-b]pyridine and
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-6-(3-cyclopentylpropyloxy)imidazo[4,5-b]pyridine.

10. A process for preparing a pharmaceutical composition useful for the treatment of gastric and/or duodenal ulcers which comprises incorporating an imidazo[4,5-b]pyridine compound as defined in claim 1 with one or more physiologically acceptable pharmaceutical carriers.

11. A process for preparing a pharmaceutical composition as claimed in claim 9 where an imidazo[4,5-b]pyridine compound is selected from the group consisting of
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-methoxtimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-methoxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-7-methoxyimidazo[4,5-b]pyridine,

2-[2-(3,4,5-trimethyl)pyridylmethylsulfinyl]-5-ethoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(3,4,5-trimethyl)pyridylmethylsulfinyl]-5-n-butyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-ethoxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-isopropyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy)pyridylmethylsulfinyl]-5-iso propyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-n-propyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy-5-methyl)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy)pyridylmethylsulfinyl]-5-isobutyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(4-methoxy)pyridylmethylsulfinyl]-5-cyclopropylmethyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-5-(2,2,2-trifluoroethoxy)imidazo[4,5-b]pyridine,
2-[2-(4-methyl)pyridylmethylsulfinyl]-5-(2,2,3,3,4,4,4-heptafluorobutyloxy)imidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-n-heptyloxyimidazo[4,5-b]pyridine,
2-[2-(3,5-dimethyl)pyridylmethylsulfinyl]-5-(3-methylbutyloxy)imidazo[4,5-b]pyridine and
2-[2-(3,5-dimethyl-4-methoxy)pyridylmethylsulfinyl]-6-(3-cyclopentylpropyloxy)imidazo[4,5-b]pyridine.

12. A process for preparing a pharmaceutical composition as claimed in claim 9 where said one or more physiologically acceptable pharmaceutical carriers are selected from the group consisting of corn starch, dextrin, α-, β- or γ-cyclodextrin, glucose, lactose, sucrose, methylcellulose, ethylcellulose, calcium carboxymethylcellulose, crystalline cellulose, magnesium stearate, sodium alginate, Witepsol W35, Witepsol E85, polyvinyl alcohol, synthetic aluminum silicate, talc, waxes, hydroxypropyl cellulose, hydroxy propyl methylcellulose, hydroxyethyl methylcellulose, cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate, polyvinyl alcohol phthalate, styrene-maleic anhydride copolymer, polyvinyl acetal diethylaminoacetate, glycerol, propylene glycol, mannitol, polyoxyethylene stearate, polyoxyethylene cetyl alcohol ether, polyethylene glycol, polyvinyl pyrrolidone, sorbitol, Tween 80, Span 60, fats, oils and water.

European Patent Office

EUROPEAN SEARCH REPORT

Application number

EP 87 30 6570

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.4)
A	EP-A-0 187 977 (OTSUKA PHARMACEUTICAL CO. LTD.) * examples 102-111, 115, 117-125; claims 16, 18-20, 22-28, 30b, 32 * & JP - A - 61 145 182 (Cat. D)	1,5,6, 8,10	C 07 D 471/04 A 61 K 31/44
A,P	CHEMICAL ABSTRACTS, vol. 106, no. 5, 2nd February 1987, page 556, column 2, abstract no. 33093t, Columbus, Ohio, US; & JP - A - 61 161 283 (KOTOBUKI SEIYAKU CO. LTD.) 21-07-1986 (Cat. A)	6	
A	GB-A-1 234 058 (EGYESULT GYOGYSZER ES TAPSZERGYAR AB) * page 1, lines 9-28; exame 15 *	6	
A	EP-A-0 134 400 (BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH)		

TECHNICAL FIELDS SEARCHED (Int. Cl.4)

C 07 D 471/00
A 61 K 31/00

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
BERLIN	13-10-1987	VAN AMSTERDAM L.J.P.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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